aeruginosa has been the sole species prone to develop imipenem resistance, achieved by loss of a specific porin, OprD. Loss of OprD also raises the MIC of meropenem, though rarely above breakpoint, but does not affect MICs of penicillins or cephalosporins. By contrast, MICs of meropenem, penicillins and cephalosporins – not those of imipenem – are raised for *P. aeruginosa* strains with increased function of the MexA-MexB-OprM multi-drug efflux system. New modes of carbapenem resistance are emerging and may present future problems: IMP-1, a plasmidic zinc β-lactamase, is spreading in gram-negative rods in Japan, and various modes of resistance occur in *Acinetobacter* spp. New carbapenems-sanfetrinem and L-749,345- are in advanced development. Sanfetrinem, an oral agent, has anti-gram positive activity resembling imipenem but is slightly less active vs. gram-negative pathogens; L-749,345 has similar activity to meropenem, except *vs. P. aeruginosa,* but has pharmacokinetics resembling ceftriaxone. Experimental carbapenems bind PBP-2′ of MRSA, and have MICs $\leq$0.03 mg/L for highly penicillin-resistant pneumococci. No described carbapenem escapes IMP-1 β-lactamase, but it may be overcome with new inhibitors.

Diagnostic mycobacteriology

S116 Current needs in mycobacteriology

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During the last decade, the industrialized nations have experienced a well-publicized tuberculosis (TB) epidemic. By the same token, the occurrence of new species of nontuberculous mycobacteria (NTM) have challenged the microbiology laboratories' capability to provide accurate results in a timely fashion. Furthermore, the economic climate puts an additional spin on the charge placed on laboratories providing clinical services. Once a diagnosis of mycobacterial disease in a patient is suspected, a series of interactions between the clinician and the laboratory are set into motion. The following three topics require attention: 1) In patients with acid-fast bacilli smear-positive sputum specimens diagnosed for the first time, the differentiation between TB and NTM is imperative (respiratory isolation, adequate drug regimen, and contact investigation); 2) in areas with increased drug resistant TB susceptibility testing results, especially for rifampin, are paramount; and 3) the emergence of clinically significant NTM, especially in immuno-comprised hosts, poses an additional challenge for patient care. The foundations of the clinical mycobacteriology laboratory of the next millennium are: a) testing and prioritizing high-quality specimens, b) joining the acid-fast network to provide accurate results in a timely fashion, and c) bridging the gap between physicians, laboratorians, and public health officials in order to improve the service rendered for our patients. As the adage goes *"That which is worth doing is worth doing right"*.

S117 Mycobacterial Screening of Non-Blood and Blood Specimens Using (Semi) Automated Mycobacteria Detection Systems

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The use of liquid media for primary isolation has always had a place in mycobacteriology. However, the inherent dangers of liquid culture (compared with solid cultures), the increased difficulties with contamination and the laboriousness of observation for signs of growth have all dictated that liquid culture be reserved for a small minority of specimens and particularly those from ordinarily sterile sites such as the spinal fluid.

Modern approaches to liquid cultures, partly driven by earlier work on non-mycobacterial organisms, have resulted in the development of automated or semi-automated liquid culture systems which are securely contained and highly selective. The addition of highly sensitive growth monitoring technology has ensured that the presence of mycobacteria in these systems can be detected at far shorter intervals than hitherto. In many instances it is now possible to grow mycobacteria, including *Mycobacterium tuberculosis,* within 2 weeks of specimen receipt.

Several different approaches have been developed. This presentation will contrast and compare these, looking particularly at the speed and accuracy of detection, the incidence of contamination, the ease of usage and the immediate usefulness of the detected liquid culture biomass for further investigations (genetic probe identifications, antibiotic susceptibilities, and so on). The presentation will also consider the optimal use for these novel but expensive methods, using data generated by a large ongoing study, and balancing issues of cost and safety against the undoubted advantages of this important advance in mycobacteriology.

S118 Drug Susceptibility Tests for *M. tuberculosis*

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Objectives: To evaluate the liquid media-based systems for rapid indirect drug susceptibility tests with *M. tuberculosis.*

Methods: New systems for mycobacterial cultivation, MB/BacT from Organon Teknika, ESP from Difco and MGIT from Becton-Dickinson, were evaluated in comparison with 7H11 agar and BACTEC-460.

Results: All methods tested are suitable for isolation of mycobacteria and for indirect susceptibility testing with *M. tuberculosis,* but the critical concentrations of some drugs require further adjustments. Timing for isolation and the indirect susceptibility test in new systems was significantly shorter than on agar plates, but it was 2 to 5 days longer than in the BACTEC-460 system.

Conclusions: Liquid media systems have the potential to expedite the diagnosis of tuberculosis and detection of drug resistance. The added cost can be justified only for initial specimens from new patients if tested in large laboratories. Indirect testing in any liquid media should not replace the direct test on 7H11 agar plates for AFB-positive specimens.

S119 Molecular technologies in diagnostic mycobacteriology

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A number of molecular techniques have recently been made available in mycobacteriology. Various key questions should be answered before routine implementation of these tools:

(a) which techniques are reliable, and for which purpose?
(b) who should perform them?
(c) will they influence patient management?
(d) are they cost-effective for the proposed setting?

A conservative position would be the following:

Goal	Technique	Laboratory Level	Efficiency
Early detection	DNA, RNA amplification	Not established	Questionable
Species identification	Accuprobe, PCR-RFLP, Sequencing	RL	Yes
Resistance testing	Genotype testing	RL in areas with MDR-TB	Yes
Epidemiology and quality control	RFLP	RL	Yes

RL: Reference Laboratory

At today's costs and limited automation, the conditions for an effective implementation of these techniques are generally only fulfilled by reference laboratories.

Towards consensus in sensitivity testing ESCMID Working Party on Antibiotic Breakpoints, Interactive Session

S120 Problems in susceptibility testing: looking for a consensus

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Antibiotic susceptibility testing varies from country to country according to the recommendations of national antimicrobial susceptibility testing committees.

Objectives: To obtain the reactions from the participating audience in order to achieve a consensus for future susceptibility testing.

Methods: This session will use an interactive audience response system to create a dynamic exchange between the audiences and the speakers. Following subjects will be covered: minimal panels for susceptibility testing for clinical use and for the surveillance of resistance mechanisms, interpretive standards for streptococci including crossresistance for betalactam antibiotics or macrolides in *S. pneumoniae*, detection of the various resistance mechanisms of enterococci, definition of breakpoints for peroral or parenteral cephalosporines, fixed or proportional ratio of betalactamase inhibitors, reporting of inducible cephalosporinase, methods to detect extended spectrum betalactamase producing enterobacteriaceae and methods to detect resistance mechanisms to fluoroquinolones. The problem of reporting susceptible organisms according to breakpoint but with a detectable resistance mechanism will be discussed. The question of optimal quality control of susceptibility testing by creating a battery of reference strains with defined resistance mechanisms covering a broader range of MIC'S will be suggested.

S121 Development of NCCLS Antimicrobial Susceptibility Testing guidelines in the global environment

M.J. Ferraro. *Mass General Hospital, Harvard Medical School, Boston, MA, USA*

NCCLS is a global association of more than 2100 organizations and institutions in 46 different countries. NCCLS standards, guidelines, products, and services promote the delivery of quality patient testing and healthcare. The NCCLS Subcommittee on Antimicrobial Susceptibility Testing is composed of representatives from microbiology laboratories, government, health care providers and educators, and pharmaceutical and diagnostic microbiology industries. Using the NCCLS consensus process, the subcommittee develops standards that promote accurate antimicrobial susceptibility testing and appropriate reporting. The Subcommittee's goals are to: 1. develop standard reference methods; 2. provide quality control parameters; 3. establish interpretive criteria; 4. provide suggestions regarding groups of antimicrobial agents for testing that encourage clinically relevant and cost-effective laboratory testing; 5. continually refine standards and optimize detection of emerging resistance mechanism through the development of new or revised methods, interpretive criteria, and quality control parameters; 6. educate users through communication of standard guidelines; and 7. foster dialogue with users of these methods and those who supply them.

The ultimate purpose of the Subcommittee's mission is to provide useful information to enable laboratories to assist the clinician inpatient care, without making recommendations concerning the clinical use of specific antimicrobial agents.

The success of the NCCLS consensus process lies, in no small measure, in the assurance that all interested parties will have a place and be heard at the table. In concert with the NCCLS'S consensus process and global growth, I welcome the opportunity to exchange views with my European colleagues and look forward to future opportunities for harmonization.

S122 Vieuwpoint of the European Industry on susceptibility testing

A. Bryskier. *Clinical Pharmacology Anti-infectives HMR, Romainville, France*

The development of antibacterial agents is divided into numerous parts: One is the microbiology section which is itself split into two sections: the first is the antibacterial spectrum and activity including break points and quality control strains, and the second is the microbiology within the clinical development (Phases II and III).

One of the main concerns for the development of antibiotics is to obtain break-points which are the baseline of the clinical development and the clinical introduction of the new antibacterial in clinical practice. The problem in Europe is very complex, some agencies promote their own break-points: France (CFA), United-Kingdom (BSAC), Sweden and Germany (DIN), other countries use NCCLS recommendations as well as recommendations from one of the above-mentioned countries.

During the Phase II/III trials, NCCLS recommendations (quality control strains, preliminary break-points) are usually used world-wide, to obtain reliable clinical and microbiological results.

After application, break-points are "delivered" by the different agencies. The most acute problems are the following: different break-points, different loads of the test disks and the quality control strains very or are not proposed. Furthermore, due to the complexity of the regulations, the variations in the load dose could be substantial among manufacturers even within different batches.

There is an acute need within the pharmaceutical industry in Europe for standardization of the methods used to determine break-points for the same quality control strains and the same load on the disks.

The NCCLS subcommittee in the USA is now establishing an alliance with the Japanese NCCLS and is currently working with the Pan America Health Organization and in Brazil.

An alliance has first to be set up in Europe and secondly with other organizations to obtain a consensus which will be help to pharmaceutical companies as well as Biodiagnostic companies.